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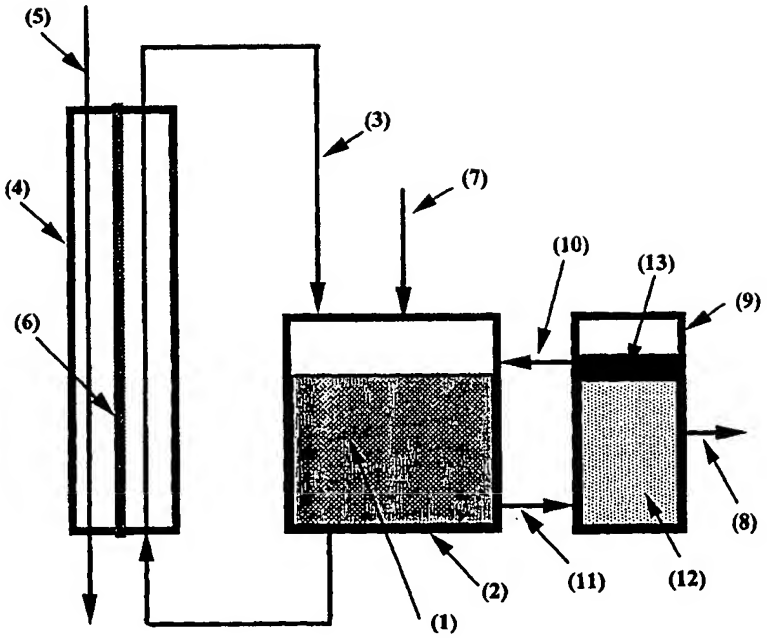
(54) Title: MEMBRANE SEPARATION INVOLVING A TWO–PHASE FLUID ON MEMBRANE SIDE

(57) Abstract

There is provided a method of transferring at least one substance across a membrane (6) from a first fluid to a second fluid, wherein transfer of the substance from the first fluid to the second fluid occurs across the membrane (6); wherein the membrane (6) comprises a non–porous membrane; and wherein either the first fluid or the second fluid is a two–phase fluid (1) which comprises at least two fluid phases (12, 13) and wherein the other of the first fluid or the second fluid is a one–phase fluid (5) which comprises at least one fluid phase.



Two-Liquid Phase Extractive Membrane Bioreactor

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MEMBRANE SEPARATION INVOLVING A TWO-PHASE FLUID ON MEMBRANE SIDE

The present invention relates to a method. In particular the present invention relates to a method of transferring at least one substance across a membrane from a first fluid to a second fluid.

Methods for contacting two liquid streams in order to effect permeation of specific chemical species between the streams are generally well known. For example, in the field of aqueous waste treatment, US-A-4,988,443 discloses a method for contacting an aqueous waste stream containing organic toxicants with a nutrient-containing aqueous stream using a porous hollow fibre membrane. The pores of the membrane are filled with water immiscible solvent. The two streams do not mix but the organic toxicants may be transferred from the waste stream across the membrane to the nutrient stream. Microorganisms growing associated with the outside of the hollow fibres utilise the nutrients and organic toxicants as growth substrates and proliferate.

Tubular elastomeric non-porous homogeneous membranes, for example tubular silicone rubber (cross linked polydimethylsiloxane), have also been disclosed. These elastomeric non-porous homogeneous membranes provide separation by allowing specific chemical species (for example, hydrophobic organic molecules such as benzene, toluene, or their derivatives) to preferentially dissolve in the membrane and permeate through the membrane by diffusion under the influence of a chemical activity driving force. For example, US-A-5,585,004 discloses a system of apparatus and method wherein a process stream containing toxic organic compounds is fed to the inside of selectively permeable silicone rubber membrane tubes suspended in a bioreactor receptacle filled with a biologically active medium containing a microbial culture. The toxic organic compounds diffuse across the silicone rubber membrane and into the biologically active medium where they are digested by the microbial culture.

A further example of the treatment of a process stream is provided by SU-A-1263654 which discloses the treatment of a process stream containing heavy metals. A microbial culture producing hydrogen sulphide is contacted with one side of a membrane, while a

process stream containing heavy metals is contacted with the opposite side. Microbially produced hydrogen sulphide permeates through the membrane and causes the metals in the wastewater to precipitate as insoluble sulphides.

In the field of gas treatment, extractive membrane systems have been used to remove organic contaminants from a gaseous stream. *Martine Reij, PhD Thesis "Membrane Bioreactor for Waste Gas Treatment", University of Wageningen* discloses systems wherein gas streams containing organic toxicants are passed on one side of either a porous or a non-porous membrane with biological culture containing medium on the other side of the membrane. Chemical species in the gas stream permeate through the membrane and are consumed by the biological culture.

WO-A-97/19196 discloses further developments. The use of combinations of membranes is disclosed wherein an organic phase acts as an absorbent to remove species from a gas process stream in one membrane module and transfer these species to a biologically active aqueous phase in another membrane module. Both porous and non-porous separating layer membranes have been reported for use in these systems where aqueous biomedium is contacted with the absorbent fluid.

Van Sonsbeek, H.M., Beeftink, H.H. and Tramper, J., "Two-liquid-phase bioreactors." Enzyme Microb. Technol., 1993, 15, p722 discloses two-liquid (aqueous-organic) phase mixture bioreactors. The aim of the bioreactor is to cause a reaction between a hydrophobic substrate dissolved in a water-immiscible organic phase and enzymes or cells in an aqueous phase. This technique has been applied to waste treatment, for example as reported by *El Aalam et al. Applied Microbiology and Biotechnology 1993, 39, p696.* El Aalam et al. discloses a technique for culture maintenance in which a hydrophobic organic substrate is first dissolved in an oil phase consisting of silicone oil or some water immiscible organic solvent in which it has a much higher solubility than its solubility in water. The oil phase is then mixed directly with the aqueous biological media, and the hydrophobic organic substrate passes from the oil phase to the aqueous phase where it is consumed by the microbial culture. The oil phase is separated from

the aqueous biological media and recirculated to a vessel in which the oil phase is replenished with hydrophobic organic substrate.

A further method reported by *Choi et al., Biotechnology and Bioengineering, 1992, 40, p1403* involves filling a silicone rubber tube with a liquid hydrophobic organic substrate (use of a mixture of benzene and toluene is disclosed) and then submerging this tube in an aqueous biological media. Silicone rubber is a hydrophobic material, and so the hydrophobic organic substrates swell the rubber and permeate across the tube wall into the biological medium where they are consumed.

It is well known that elastomers such as rubbery polymers swell when contacted with solutions whose molecules are able to dissolve in the polymer matrix. For example, silicone rubber will swell in contact with pure organic phases (for example toluene, mineral oil, alkanes, aromatics, silicone oil) or mixtures thereof. Natural rubber will swell in contact with organic solvents. The permeation of molecules across swollen elastomer membranes has been studied in detail, see for example *Paul D.R. and Ebra-Lima O.M., Journal of Applied Polymer Science, 1975, 19 , p2759.* Molecules can permeate through an elastomer swollen with a solvent liquid or oil, under the influence of a pressure or concentration driving force.

The extractive membrane bioreactor technology of the prior art has various disadvantages.

One disadvantage is the attachment and growth of biofilms on the surfaces of the membrane being employed.

Some prior art teachings, for example US-A-4,988,443, teach towards encouraging cell growth on the walls of the membrane. Other teachings, for example *Freitas dos Santos L.M. and Livingston A.G. "Membrane Attached Biofilms for VOC Treatment. II: Effect of Biofilm Thickness on Performance", Biotechnol. Bioeng., 42, (1995), p90-95*; and *Martine Reij, PhD Thesis "Membrane bioreactor for waste gas treatment", University*

of Wageningen, propose that biofilm growth can lead to large reductions in fluxes of the specific chemical species being transferred across a membrane. It is believed that the reduction in flux occurs because the biofilm can form a stagnant layer through which the transferring species and/or oxygen must diffuse before they can react. *Pavasant P., Freitas dos Santos L.M., Pistikopoulos E.N. and Livingston A.G. "Prediction of Optimal Biofilm Thickness for Membrane Attached Biofilms", Biotechnol. Bioeng., 52, (1996), p373-386* teaches that biofilms in excess of 200-500 μm in thickness can reduce the flux of transferring species through the membrane by an order of magnitude. The implication of this level of flux reduction for the industrial utility of extractive membrane bioreactor processes is important - as membrane flux falls, more membrane area is required and so both the capital costs of providing the membrane area and the operating costs of pumping the process stream through the membrane, increase.

Attachment of biomass to surfaces to form biofilms is a well known phenomenon. There has been considerable scientific effort dedicated to investigating why biofilms form, and to developing methods for controlling or eliminating biofilms. It is generally accepted that biomass attaches to surfaces due to a combination of surface properties, electrostatic and hydrophobic forces. Methods developed for removing or eliminating biofilms include coating surfaces with materials to which biomass does not stick, addition of oxidising or non-oxidising biocides to the biomedium, and chemical and mechanical treatments, see *Characklis W.G. and Marshall K.C. "Biofilms" (1990) John Wiley and Sons, New York.* However, none of these methods has found practical application in extractive membrane bioreactor processes.

The avoidance of biofilm formation in extractive membrane bioreactor systems remains a problem of prior art systems.

The present invention seeks to address the problems of the prior art.

The present invention aims to provide a method to control or avoid the formation and growth of biofilms on membranes. Specifically, the present invention aims to provide a

method to control or avoid the formation and growth of biofilms on membranes for use in extractive membrane bioreactor systems.

In a first aspect the present invention provides a method of transferring at least one substance across a membrane from a first fluid to a second fluid, wherein transfer of the substance from the first fluid to the second fluid occurs across the membrane; wherein the membrane comprises a non-porous membrane; and wherein either the first fluid or the second fluid is a two phase fluid which comprises at least two fluid phases and which comprises a biological material selected from microbial cells, enzymes, biocatalysts, derivatives and mixtures thereof; and wherein the other of the first fluid or the second fluid is a one phase fluid which comprises at least one fluid phase.

The term "non-porous membrane" is well known in the art. The term is analogous to the terms "dense membrane" and/or "dense phase membrane".

The present invention provides a method wherein there is substantially less biofilm development and/or substantially better mass transfer than in a conventional extractive membrane bioreactor system.

The two phase fluid comprises a first fluid phase (Phase A) and a second fluid phase (Phase B).

Without being bound by theory, it is believed that these advantages are achieved because biological material is attracted to the interface between Phase A and Phase B, and so is relatively less attracted to the interface between the two phase fluid and the membrane.

The decrease or total absence of biofilm formation which may be provided by the present invention improves extractive membrane bioreactor utility since the flux across the membrane is maintained at higher values.

The invention provides an effective means for controlling the formation of biofilms.

In a second aspect the present invention provides the use of a non-porous membrane to transfer at least one substance across the membrane from a first fluid to a second fluid, wherein transfer of the substance from the first fluid to the second fluid occurs across the membrane; wherein the membrane comprises a non-porous membrane; and wherein either the first fluid or the second fluid is a two phase fluid which comprises at least two fluid phases and which comprises a biological material selected from microbial cells, enzymes, biocatalysts, derivatives and mixtures thereof; and wherein the other of the first fluid or the second fluid is a one phase fluid which comprises at least one fluid phase.

Preferably, Phase A is aqueous based. More preferably, Phase A comprises an aqueous medium containing the biological material. In this aspect, it is preferred that Phase B is non-inhibitory to the biological material.

Preferably, Phase B comprises a substantially water immiscible phase. Preferably, the substantially water immiscible phase is selected from an organic solvent, such as hexadecane, octanol, decanol, tetradecane, hexadecanol, benzene, toluene and including fluorinated organic solvents, such as perfluoromethyldecalin; an oil such as mineral oil, kerosene, sunflower oil; a high molecular weight organic compound such as polyethylene glycol; an inorganic oil such as silicone oil; derivatives and mixtures thereof.

When Phase B comprises a substantially water immiscible phase the present invention is particularly advantageous because biofilm formation is further decreased. Without being bound by theory, it is believed that this is because the non-porous membrane becomes swollen by the presence of substantially water immiscible phase - swollen polymers may be less attractive sites for microbial adsorption. Moreover, swelling of the non-porous membrane reduces membrane resistance and improves mass transfer relative to a non-swollen non-porous membrane.

Preferably, Phase B is selected such that the at least one substance, preferably which is to be transferred from the one phase fluid to the two phase fluid, has a partition coefficient (defined below) of from 1 to 10000, more preferably of from 10 to 10000.

$$\text{Partition coefficient} = \frac{\text{concentration of substance in Phase B}}{\text{concentration of substance in Phase A}}$$

Preferably, Phase B may be readily separated from water or Phase A.

In a preferred embodiment Phase A and Phase B are mixed so that one of Phase A and Phase B forms a continuous phase in the two phase fluid and the other of Phase A and Phase B forms a dispersed phase in the two phase fluid.

The two phase fluid may be formed by mixing Phase A and Phase B directly so that either Phase A or Phase B forms small droplets in the other phase (the phase forming droplets is said to be the dispersed phase, while the phase not forming droplets is said to be the continuous phase).

The two phase fluid may be an emulsion.

Preferably, Phase B is added to Phase A so that the phase ratio, defined below, is from 0.1 and 10.

$$\text{Phase ratio} = \frac{\text{volume Phase B}}{\text{volume Phase A}}$$

Preferably, the one phase fluid is liquid or gaseous. More preferably, the one phase fluid is liquid. Yet more preferably, the one phase fluid is aqueous liquid or gaseous. For example the one phase fluid may be an aqueous liquid containing hydrophobic organic compounds, an aqueous liquid containing heavy metals, a gas stream containing

one or more organic compounds, or an organic stream containing a mixture of hydrophobic and hydrophilic organic compounds.

Preferably, the one phase fluid contains a metal.

Preferably, the at least one substance is either consumed by or produced by a biological material selected from microbial cells; enzymes, biocatalysts, derivatives and mixtures thereof.

The at least one substance may be transferred from the one phase fluid to the two phase fluid, or may be transferred from the two phase fluid to the one phase fluid. Preferably, the at least one substance is transferred from the one phase fluid to the two phase fluid.

Preferably, the at least one substance is consumed in the fluid into which it is transferred. In a preferred embodiment the at least one substance is transferred from the one phase fluid to the two phase fluid in which it is consumed, preferably by a biological material.

Preferably, the at least one substance is a hydrophobic organic substrate.

Preferably, the at least one substance is a product of a biological material selected from microbial cells, enzymes, biocatalysts, derivatives and mixtures thereof.

The at least one substance may be/comprise hydrogen sulphide. In this aspect the at least one substance is preferably transferred from the two phase fluid to the one phase fluid.

The at least one substance may be/comprise an organic compound(s). In this aspect the at least one substance is preferably transferred from the one phase fluid to the two phase fluid.

The at least one substance, preferably which is transferred from the one phase fluid to the two phase fluid, will, in a preferred aspect of the present invention, dissolve in Phase B in preference to Phase A. This may be advantageous because dissolution of the at least one substance in Phase B will be followed by eventual further transfer of the substance from Phase B to Phase A and thus the two phase fluid will be buffered and the entry of the at least one substance into Phase A will be regulated. This is particularly advantageous when the at least one substance is toxic or inhibitory at high concentrations to biological material present in Phase B. Moreover, buffering assists operation when a sudden loading change due to fluctuations in flowrates or concentrations of the one phase fluid occurs.

Preferably, the two phase fluid is contained in a bioreactor. More preferably, nutrient (preferably an aqueous nutrient composition) is added to the two phase fluid in the bioreactor. Thus biological material which may be present in the two phase fluid is replenished with nutrients and growth factors. The addition of nutrient may create an overflow from the bioreactor. Preferably, the overflow is removed as an aqueous overflow stream. The overflow may be treated/handled by a phase separator connected to, or integral with, the bioreactor. The phase separator may serve to separate Phase A and Phase B present in the overflow. Phase A may be withdrawn from the separator as waste (a waste stream) and/or separated. Phase B may be returned to the bioreactor.

Thus, in a preferred embodiment, the two phase fluid is contained in a bioreactor comprising at least a first zone and a second zone, wherein the first zone is discreet from the second zone;

wherein the first zone and the second zone are operably connected to each other;

wherein the first zone contains the first fluid and the second fluid ;

and wherein at least a portion of the two phase fluid may be transferred to the second zone wherein nutrient is added and/or at least one of the two phases is separated from the two phase fluid.

Preferably the nutrient is nutritious to biological material.

It is essential that the membrane comprises a non-porous membrane. Suitable membranes may be constructed many ways. For example the membrane may be a composite membrane comprising a porous component, preferably a support, and a non-porous membrane component.

Preferably, the non-porous membrane is selected from lipophilic dense phase materials including hydrophobic polymers. More preferably the non-porous membrane is selected from polydimethylsiloxane (PDMS) based elastomers, other modified polysiloxane based elastomers, ethylene-propylene diene (EPDM) based elastomers, polynorbornene based elastomers, polyoctenamer based elastomers, polyurethane based elastomers, butadiene and nitrile butadiene rubber based elastomers, natural rubber, butyl rubber based elastomers, polychloroprene (Neoprene) based elastomers, epichlorohydrin elastomers, polyacrylate elastomers, polyethylene, polypropylene, polytetrafluoroethylene (PTFE), polyvinylidene difluoride (PVDF), derivatives and mixtures thereof.

In the aspect wherein the membrane comprises a porous material, the porous material is preferably selected from ceramic materials including zeolites; polymeric materials suitable for use in fabricating microfiltration, ultrafiltration, nanofiltration or reverse osmosis membranes, including polyethylene, polypropylene, polytetrafluoroethylene (PTFE), polyvinylidene difluoride (PVDF), polyetherimide (PEI), polyethersulfone; derivatives and mixtures thereof. The porous material may be selected such that the pores are arranged to provide porosity in respect of the first fluid and/or the second fluid, depending on which provides superior performance.

An external surface of the membrane may be braided with a support material such as by way of non-limiting example mesh comprising metal wire, polymer strands, or natural or synthetic cotton. Braiding will increase the strength of the membrane. This is particularly important in some applications in which the membrane will contact pure solvent phases which may weaken the non-porous membrane.

The membrane may consist essentially of a single non-porous membrane.

The membrane may comprise one or more sections. The one or more sections of the membrane may comprise one or more membrane materials independently of each of other. Preferably the membrane material of each of the one or more sections is independently selected from the membrane materials described above.

Preferably, the membrane is contained in a shell or a module. The membrane modules may be of any design known to those skilled in the art, such as spiral wound, plate and frame, shell and tube, and derivative designs thereof.

The membrane may be of cylindrical or planar geometry. Preferably, the membrane partially or completely defines an internal volume and an external volume. Preferably, the membrane is a hollow fibre/tubular membrane.

When a hollow fibre/tubular membrane is used, either the first fluid or the second fluid may be held within the internal volume of the membrane provided the other of the first fluid and the second fluid is in contact with an external surface of the membrane.

Preferably, the one phase fluid is held within the internal volume of a tubular membrane.

Preferably, the two phase fluid is held within the internal volume of a tubular membrane.

Preferably, the membrane partially or completely defines an internal volume and two distinct external volumes. In this aspect a third fluid may be held within the internal volume; and either the first fluid or the second fluid held within one of the external volumes in contact with an external surface of the membrane, and the other of the first fluid and the second fluid held within the other external volume in contact with an

external surface of the membrane.

Alternatively, the membrane partially or completely defines an external volume and two distinct internal volumes. In this aspect a third fluid may be held within the external volume; and wherein either the first fluid or the second fluid held within one of the internal volumes in contact with an internal surface of the membrane, and the other of the first fluid and the second fluid held within the other internal volume in contact with an internal surface of the membrane.

The invention will now be described, by way of example only, with reference to the accompanying drawings, in which:-

Figure 1 shows a system for use in accordance with the method of the present invention.

Figure 2 shows a system for use in accordance with the method of the present invention.

Figure 3 shows a system for use in accordance with the method of the present invention.

Figure 1 shows an extractive membrane bioreactor system configured in accordance with the present invention. A two phase fluid (1) is recirculated (3) from a bioreactor (2) through a membrane module (4) where it is contacted with one side of a membrane with a dense (non-porous) separating layer (6). A one phase fluid (process stream) (5) is contacted with the other side of the membrane (6). A nutrient stream (7) is added to the bioreactor (2) to replenish the biological material with nutrients and growth factors. A flow of the two phase fluid (11) will pass into a phase separator (9) and divide into two continuous phases, Phase A (12) and Phase B (13). Separated Phase B will be returned to the bioreactor from the separator (10). Corresponding to the nutrient stream (7) an overflow stream of Phase A (8) is withdrawn from the phase separator (9) connected to the bioreactor (2). In general the apparatus will be arranged so that the liquid level in the bioreactor (2) remains constant.

The biomedium (Phase A), will in general comprise water with minerals, vitamins or organics added as required to support biological growth and reaction. The biocatalyst present in the biomedium will be cells or enzymes or other biocatalysts. The biocatalysts may consume oxygen, organics, or produce hydrogen sulphide, organics, or other materials. The bioreactor can be any vessel or receptacle in which the biocatalysts can be effectively employed and in which the two phase fluid can be effectively formed through mixing of Phase A and Phase B. In one embodiment, Phase A and Phase B can be mixed externally to the bioreactor, for example using an in-line mixer or static mixer, or any other device known to those skilled in the art.

Permeation of fluids across non-porous separating layers is known to occur when a pressure driving force exists. Permeation of Phase B or Phase A under an induced pressure driving force between the process stream and the two phase fluid can occur through the dense separating layer when the two phase fluid is at a higher pressure on one side of the membrane than the one phase fluid on the other side of the membrane. This can be exacerbated if the non-porous separating layer is swollen by the presence of Phase B. It is generally undesirable for Phase B to appear in the wastewater as a free phase and in these cases the pressure drops of both fluid streams in the membrane module should be carefully controlled. Whether careful control is necessary or not will depend in part on the phase ratio, on whether phase A or phase B is the dispersed phase in the two phase fluid, and on the extent to which Phase B swells the membrane. In general, high phase ratios, Phase B continuous systems, and extensive swelling of the membrane by Phase B will lead to greater potential for permeation of Phase B to the one phase fluid and to a requirement for more careful pressure control. For the method shown in Figure 1 it will be desirable in many cases for the pressure of the one phase fluid to be greater than the pressure of the two phase fluid at any given position in the module where the two fluids are on opposite sides of a membrane.

An alternative method for controlling phase B breakthrough is shown in Figure 2. The concept of a contained liquid membrane (CLM) is known (*Ho W.S. and Sirkar K.K "Membrane Handbook", 1992, Van Nostrand Reinhold, New York*). CLM systems

comprise two membranes with a fluid interspersed between them. In the present invention, a CLM can be employed as follows.

Two membranes are held in a module so that the process stream (5) can pass one surface of membrane A (21), and the two phase fluid can pass on one surface of membrane B (22). In between membranes A (21) and B (22) a cavity (24) is filled with Phase C (23). The two phase fluid(3) flows across the surface of membrane B (22), and is at a higher pressure than Phase C (23) in the cavity (24). The one phase fluid(5) flows across the surface of membrane A (21) and is at a higher pressure than Phase C (23) in the cavity (24). The cavity (24) is preferably held near atmospheric pressure. Under the influence of the pressure driving force between the two phase fluid and Phase C, some of the Phase B or Phase A present in the two phase fluid(3) may permeate through membrane B (22) and into the cavity (24). However, since the one phase fluid(5) is also at a higher pressure than Phase C in the cavity (24), there is no permeation of Phase B or Phase A or Phase C across membrane A (21). Any Phase B or Phase A which permeates across membrane B (22) , may be disposed of as excess or recycled to the bioreactor (2). Under the influence of the pressure driving force between the one phase fluid(5) and Phase C (23), some of the material in the one phase fluid may permeate through membrane A (21) and into the cavity (24) . If this material accumulates in Phase C (23) or in the cavity (24), it may be disposed of as excess or recycled to the bioreactor or to the one phase fluid.

One preferred embodiment of the CLM system is shown in Figure 3. Tubular membranes are used for membrane A (25) and membrane B(26). The cavity surrounding these tubular membranes in the module (24) is filled with Phase C (23). The one phase fluid (5) and the two phase fluid (3) are pumped through the insides of membranes A (25) and B (26) respectively. The module shell cavity (24) filled with Phase C (23) is maintained at or near atmospheric pressure. This mode of operation ensures that the pressures in the membranes tubes (25) and (26) will be higher at any point than the pressure in the cavity (24) filled with Phase C (23).

In the CLM system Phase C will preferably have a high partition coefficient (i.e from 1 to 10000 as defined above) for the species being transferred between the one phase fluid and the two phase fluid. Phase C may be of substantially the same material as Phase B. The membranes will have a non-porous separating layer and will preferably be of same materials as the membranes described above.

EXAMPLES

Example 1

(with reference to Figure 1): An aqueous process stream (one phase fluid) containing an organic compound (monochlorobenzene) was passed on the inside of a membrane tube. The membrane used was a 3 mm internal diameter, 4.2 mm external diameter silicone rubber tube. A two phase fluid, containing water, microorganisms and nutrients (Phase A), and silicone oil (Phase B), was passed on the outside of the membrane tube. The phase ratio was 3. The organic compound present in the process stream diffused across the elastomeric membrane and was consumed by the microorganisms in the two phase fluid, thus maintaining the driving force for the mass transfer. The mass transfer coefficient was maintained at a value of over 1×10^{-5} m s^{-1} over 7 days. Data for the same system but without a two phase fluid in the bioreactor showed that the mass transfer coefficient fell to less than 0.5×10^{-5} m s^{-1} within five days.

Example 2

(with reference to Figures 1 and 3): An aqueous process stream (one phase fluid) containing an organic compound (monochlorobenzene) was passed on the inside of a membrane tube (membrane A (25)). A two phase fluid, containing water, microorganisms and nutrients (Phase A), and silicone oil (Phase B), was passed on the inside of a second membrane tube (membrane B (26)). The phase ratio was 3. The membrane tubes used were 3mm internal diameter, 4.2 mm external diameter silicone rubber tubes. The module shell side cavity (24) was filled with silicone oil (23). The organic compound present in the process stream diffused across membrane A (25), into the silicone oil (23), and then across membrane B (26) and into the recirculating two

phase fluid (3), where it was consumed by the microorganisms, thus maintaining the driving force for the mass transfer. The mass transfer coefficient was maintained at a value of over 3×10^{-5} m s^{-1} over 3 weeks. Data for the same system but without a two phase fluid in the bioreactor showed that the mass transfer coefficient fell to less than 0.5×10^{-5} m s^{-1} in within 5 days.

Modifications of the present invention will be apparent to those skilled in the art.

CLAIMS

1. A method of transferring at least one substance across a membrane from a first fluid to a second fluid, wherein transfer of the substance from the first fluid to the second fluid occurs across the membrane; wherein the membrane comprises a non-porous membrane; and wherein either the first fluid or the second fluid is a two phase fluid which comprises at least two fluid phases and which comprises a biological material selected from microbial cells, enzymes, biocatalysts, derivatives and mixtures thereof; and wherein the other of the first fluid or the second fluid is a one phase fluid which comprises at least one fluid phase.

2. A method according claim 1 wherein the two phase fluid comprises an aqueous phase and a substantially water-immiscible phase.

3. A method according to claim 1 or 2 wherein the at least one substance is either consumed by or produced by a biological material selected from microbial cells, enzymes, biocatalysts, derivatives and mixtures thereof.

4. A method according to claim 3 wherein the at least one substance is a product of a microbial cell, enzyme and/or biocatalyst.

5. A method according to any one of the preceding claims wherein the two phase fluid is contained in a bioreactor comprising at least a first zone and a second zone, wherein the first zone is discreet from the second zone;
wherein the first zone and the second zone are operably connected to each other;
wherein the first zone contains the first fluid and the second fluid ;
and wherein at least a portion of the two phase fluid may be transferred to the second zone wherein nutrient is added and/or at least one of the two phases is separated from the two phase fluid.

6. A method according to any one of the preceding claims wherein the at least one

substance is transferred from the one phase fluid to the two phase fluid and is consumed in the two phase fluid.

7. A method according to any one of the preceding claims wherein the at least one substance is a hydrophobic organic substrate.

8. A method according to any one of the preceding claims wherein the at least one substance is hydrogen sulphide.

9. A method according to any one of the preceding claims wherein the one phase fluid comprises a metal.

10. A method according to any one of the preceding claims wherein the membrane consists essentially of a single non-porous membrane material.

11. A method according to any one of claims 1 to 9 wherein the membrane consists essentially of a composite membrane, and wherein the composite membrane comprises at least two layers, at least one of which comprises a non-porous membrane material.

12. A method according to any one of the preceding claims wherein the membrane partially or completely defines an internal volume and two distinct external volumes; wherein a third fluid is held within the internal volume; and wherein either the first fluid or the second fluid is held within one of the external volumes in contact with an external surface of the membrane, and the other of the first fluid and the second fluid is held within the other external volume in contact with an external surface of the membrane.

13. A method according to any one of claims 1 to 11 wherein the membrane partially or completely defines an external volume and two distinct internal volumes; and wherein a third fluid is held within the external volume; and wherein either the first fluid or the second fluid is held within one of the internal volumes in contact with an internal surface of the membrane, and the other of the first fluid and the second fluid is held

within the other internal volume in contact with an internal surface of the membrane.

14. A method according to any one of the preceding claims wherein the membrane is a tubular membrane.

15. A method according to claim 14 wherein the tubular membrane is contained in a shell.

16. A method according to claim 14 or 15 wherein the one phase fluid is held within the internal volume of the tubular membrane.

17. A method according to claim 14 or 15 wherein the two phase fluid is held within the internal volume of the tubular membrane.

18. A method according to any one of the preceding claims wherein the one phase fluid is a liquid.

19. A method according to any one of claims 1 to 17 wherein the one phase fluid is a gas.

20. Use of a non-porous membrane to transfer at least one substance across the membrane from a first fluid to a second fluid, wherein transfer of the substance from the first fluid to the second fluid occurs across the membrane; wherein the membrane comprises a non-porous membrane; and wherein either the first fluid or the second fluid is a two phase fluid which comprises at least two fluid phases and which comprises a biological material selected from microbial cells, enzymes, biocatalysts, derivatives and mixtures thereof; and wherein the other of the first fluid or the second fluid is a one phase fluid which comprises at least one fluid phase.

21. A method as substantially described herein and with reference to any one of Figures 1-3.

22. A use as substantially described herein and with reference to any one of Figures 1-3.

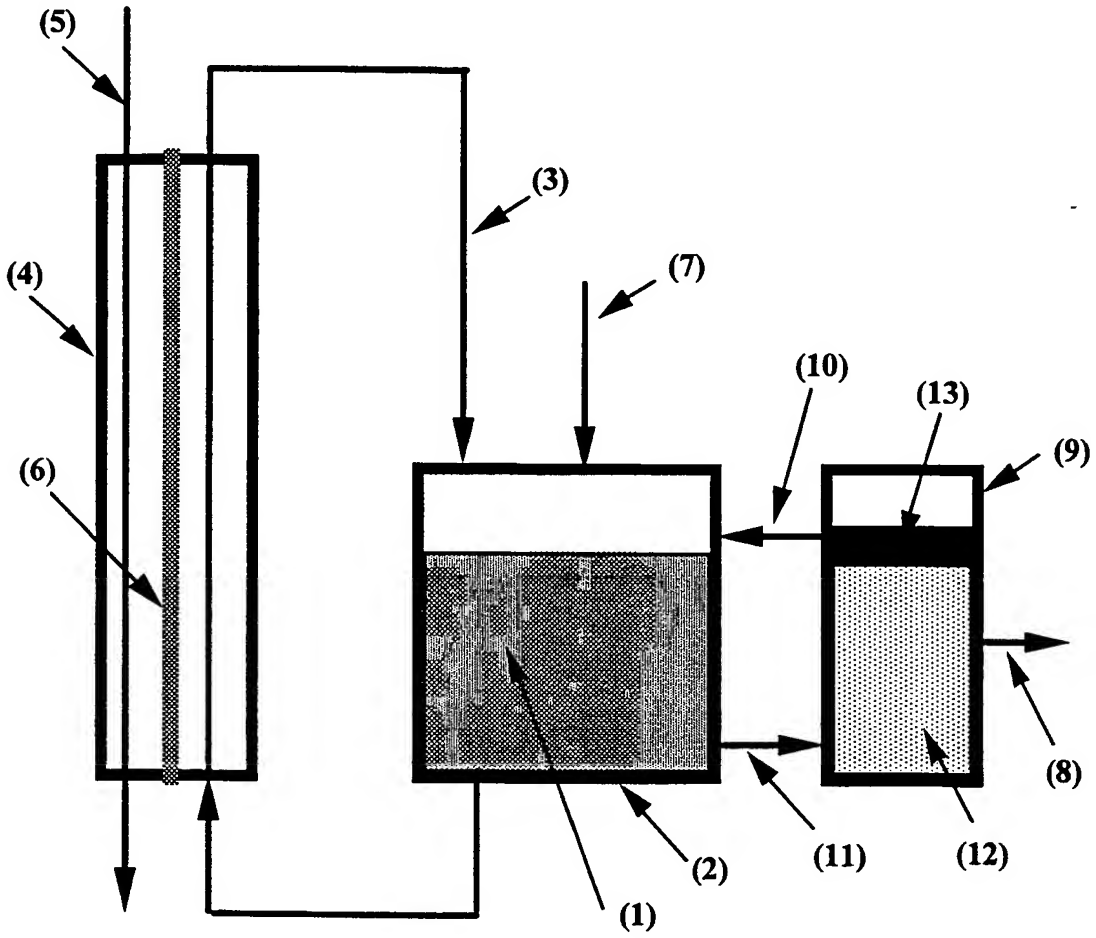

Figure 1 - Two-Liquid Phase Extractive Membrane Bioreactor

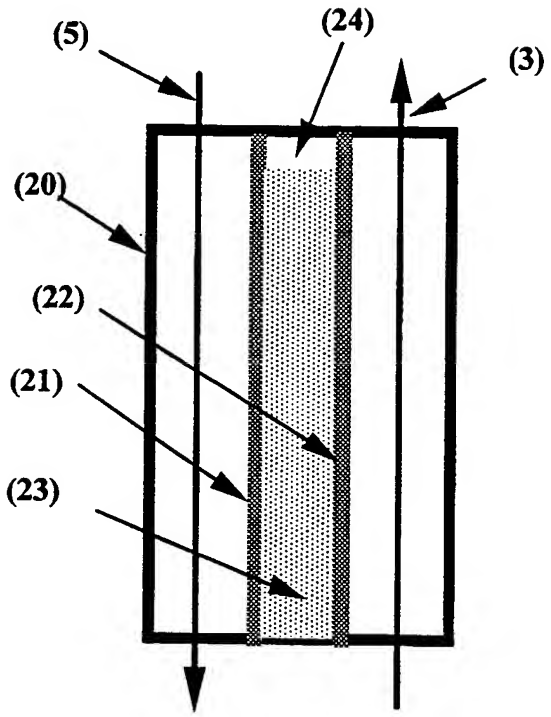

Figure 2 - CLM System (General)

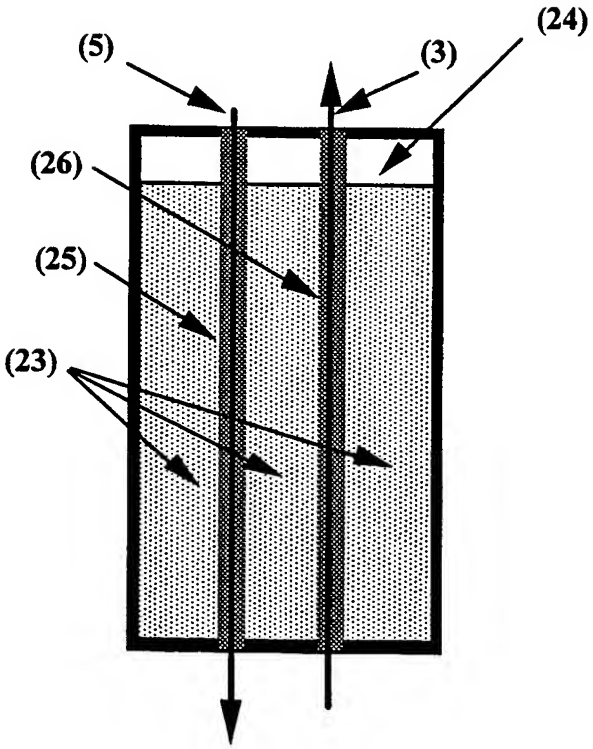

Figure 3 - CLM System (Tubular)

INTERNATIONAL SEARCH REPORT

Intern[illegible]lication No
PCT/GB 99/02011

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01D61/24 B01D61/38 B01D61/36 B01D53/84 C02F1/44
C12M3/06 C12M1/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01D C02F C12M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 41 16 426 A (FRAUNHOFER GES FORSCHUNG) 19 November 1992 (1992-11-19) column 1, line 3 - line 6 column 3, line 42 - column 6, line 67 column 7, line 47 - column 8, line 16; claims 1,3; examples 1,3	1-5,7, 10,11, 18,20-22
A	WO 97 19196 A (UNIV NORTH CAROLINA) 29 May 1997 (1997-05-29) cited in the application page 5, line 4 - page 6, line 5 page 7, line 8 - page 8, line 24 page 10, line 3 - line 22; figures 1,2	1-22

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
21 September 1999	28/09/1999

Name and mailing address of the ISA	Authorized officer
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 26806 A (IMPERIAL COLLEGE ;LIVINGSTON ANDREW (GB); FREITAS DOS SANTOS LUISA) 12 October 1995 (1995-10-12) claims 1-13; figures 3,5-7 ---	1-22
A	WO 96 18719 A (IMPERIAL COLLEGE ;LIVINGSTON ANDREW (GB); BOAM ANDREW TIMOTHY (GB)) 20 June 1996 (1996-06-20) page 9, line 6 - page 14, line 15; claims 1-10; figures 1,1A,3,5,11A,12 -----	1-22

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 4116426 A	19-11-1992	NONE	
WO 9719196 A	29-05-1997	AU 1122097 A	11-06-1997
		CA 2238323 A	29-05-1997
		EP 0906450 A	07-04-1999
WO 9526806 A	12-10-1995	AU 2080795 A	23-10-1995
		EP 0752909 A	15-01-1997
		JP 9510917 T	04-11-1997
WO 9618719 A	20-06-1996	AU 4267296 A	03-07-1996